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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,281	10/13/2000	Hyun Kim	GI 5387	9127

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EXAMINER	
HARLE, JENNIFER I	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/687,281	KIM ET AL.	
	Examiner	Art Unit	
	Jennifer I. Harle	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 11-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14 and 16* is/are allowed.

6)☒ Claim(s) *1-7,11-13,15,17-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7 and 11-16 are pending. Claims 8-10 are canceled. Claims 17-27 are newly presented in Applicant's Amendment, filed August 4, 2004. All previous Office Actions and arguments are incorporated by reference.

Specification

Claim 17 is objected to because of the following informalities: after (b) "in" should be "an". Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7 and 11-13 remain rejected and new claims 17-18 and 20-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valentini, et al. (US 5,939,974) in view of Pheulpin (US 3,955,719), Langen, et al. (US 4,784,055) and Phillips, et al. (US 4,758,233).

Applicants' argue that the 35 U.S.C. 103 (1) rejection as obvious over Valentini in view in view of Pheulpin, Langen, and Phillips should not be persuasive because evidence submitted in the form of the Declaration made by Dr. Hyun Kim has demonstrated that the substance in the Valentini patent cannot be injected through the skin as required by the pending claims despite the Examiner's arguments to the contrary. Applicants' arguments are two-fold: 1) the references only teach that pastes are injectable and 2) the composition contains pore formers and none of the documents disclose that such compositions would be injectable at all let alone through the

skin. Applicants' argue that Pheulpin, Langen and Phillips describe devices for the injection of pastes and liquids, i.e. Pheulipin for injection of pastes into dental cavities, Langen pastes into a meat, and Phillips injection of a medicament in the form of a cream or paste.

However, the Examiner noted the deficiencies of the Kim declaration, in the Final Office Action, that he did not agree that liquids have a porosity but rather solids do and that the porosity discussed in Valentini is the final product that results from curing the liquid intermediate. This was never disputed nor argued by the Applicants. Moreover, it is noted that the example specifically states that "[T]he quantity used in each experiment, therefore was adjusted in order to produce a scaffold having the desired porosity, pore distribution, and interconnectivity .... The final scaffold pore size is dependent on the size of the NaCl crystals used and, therefore, the size of the NaCl crystals to be used was determined based on the desired pore size." (col. 8, lines 35-43 – the same sections referred to in the Kim Declaration) The disclosure further discloses that the porous scaffolds of the invention can be fabricated to any size or shape and can be produced to virtually and desired predetermined pore size depending upon the application (col. 2, lines 7-10). The Examiner further rebutted the declaration's contention of non-injectability by stating that even a thick past is injectable given 1) a larger needle, and 2) a means to force the paste through the needle, i.e. the latter is readily accomplished by a device like a caulking gun.

Additionally, the instant claims are drawn to a composition having functional intended use. As previously noted, the scaffolding is formed from mixed solution by drying from the wet state, preferably by lyophilization without freezing (col. 7, lines 22-24). Thus, it is clear that prior to drying, Valentini discloses a solution that meets the limitations of the instant claims. The same preferred hyaluronic acid esters - HYAFF®, the same pore-forming agents, the same

tricalcium phosphate and several of the same BMPs, and the same solubilizing organic solvents are explicitly recited as being parts of this composition. There is no indication that the solutions are not injectable, just that it is preferred tot dry the solutions to form an implantable porous scaffold.

Moreover, Valentini discloses that the preferred hyaluronic derivative is 100% esterified hyaluronic acid-benylcovalent conjugates sold under the trade name HYAFF, thus claims 22-27 are rejected as disclosed by Valentini.

Claim 17-18 and 20-21are rejected for the same reasons set forth in claims 1-5, 7 and 11 and 13.

Applicants' arguments filed 4 August 2004 have been fully considered but they are not persuasive. The rejection is maintained for the reasons of record and the additional reasons set forth above **and made final**.

Claims 6 and 15 remain rejected and new claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Valentini, et al. (US 5,939,974) in view of Wozeney et al. (US (6,187,742) in further view of Pheulpin (US 3,955,719), Langen, et al. (US 4,784,055) and Phillips, et al. (US 4,758,233).

Applicants' argue the same arguments as set forth above in regards to Valentini. See the response set forth above. Applicants' Response concedes that Wozeney describes the use of BMP-7 in pharmaceutical compositions comprising hyaluronic acid but claims that it does not disclose injectable formulations. However, as previously noted, "Instead, the protein of the present invention, in a suitable buffer such as that described above, is applied directly to the site in need of tissue repair. For, example, the protein may be applied using a brush or other suitable

applicator **such as a syringe for injection.**"[1] Thus, Applicants' argument is not persuasive. As previously noted Wozeney discloses the combination of osteogenic proteins (including (BMP-7, which is OP-1), and preferably BMP-2); col. 3, lines 26-50), with a number of carriers, including porous particulate polymers (including PEG; cols. 4-5, lines 59-5), sucrose (col. 5, lines 40-42), hyaluronic acid and tricalcium phosphate (col. 5, lines 50-56), as well as the use of the preparation by injection through a syringe (col. 5, line 63) and the use of BMP-12 (col. 3, lines 27-32, col. 4, lines 1-5, claims 5, 7, 12).

Claim 19 is rejected for the same reasons set forth in claim 15.

Applicants' arguments filed 4 August 2004 have been fully considered but they are not persuasive. The rejection is maintained for the reasons of record and the additional reasons set forth above **and made final**.

Allowable Subject Matter

Claims 14 and 16 are allowed because they have been rewritten in independent form, including all of the limitation of the base claim and any intervening claims.

The reasons for allowance was previously set forth in the prior Office Action and is set forth again below:

Claims 14 and 16 require that the hyaluronic acid ester is Hyaff11p65. This ester does not appear to have been known in the art prior to the instant disclosure, see Campoccia, et al. (1998) and Radice, et al. (US 6,6699,471), and was not disclosed in a publication until WO 03/099992 (all previously cited). Given that the instant disclosure provides evidence of the advantage of this ester over other known Hyaff11 esters disclosed in Valentini, a rejection as

[1] Other materials which may be suitable for use as carriers for BMPs in the methods and compositions of the present

obvious under 103 would not be sustainable and was not made. While della Valle, et al. (US 4,581,521) discloses methods of preparing various full and parital hyaluronic acid ester including benyls used in Hyaff11, they do not explicitly disclose or reasonably suggest this particular ester or its advantages as instantly disclosed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer I. Harle whose telephone number is (571) 272-2763. The examiner can normally be reached on Monday through Thursday, 6:30 am to 5:00 pm,.

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invention include hyaluronic acid ..., i.e. can be used in the buffer. (col. 5, lines 36-53).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer Ione Harle
October 13, 2004

MICHAEL MELLER
PRIMARY EXAMINER